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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/001,725	10/22/2001	Kevin Pan	ORT-1517	7498
27777	7590	03/16/2004	EXAMINER	
PHILIP S. JOHNSON JOHNSON & JOHNSON ONE JOHNSON & JOHNSON PLAZA NEW BRUNSWICK, NJ 08933-7003			HUANG, EVELYN MEI	
			ART UNIT	PAPER NUMBER
			1625	

DATE MAILED: 03/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.

10/001,725

Applicant(s)

PAN ET AL.

Examiner

Evelyn Huang

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 23 February 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
- ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 23 February 2004. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3. ☒ Applicant's reply has overcome the following rejection(s): see attachment.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☒ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attachment.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

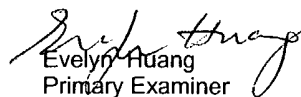
The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: 5 and 7-9.Claim(s) rejected: 1-4, 10, 12-20.

Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____.
10. ☐ Other: _____


Evelyn Huang
Primary Examiner
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Attachment to Advisory Action

1. 1-5, 7-10, 12-20 are pending. Claim 6 has been canceled according to the amendment filed on 7-1-2003. Claim 11 has been canceled according to the amendment filed on 2-23-2004.
2. Applicant mentioned in the Remarks that the examiner had made the previous action (mailed on 9-23-2003) Final, however, the last office action was a non-final action. Since Applicant has filed a Notice of Appeal, this action is an advisory action.

Duplicate Claims

3. The objection to Claim 11 as being a substantial duplicate of claim 10 would be rendered moot by the cancellation of claim 11.

Claim Rejections - 35 USC § 103

4. The rejection for Claims 1-4, 10, 12 under 35 U.S.C. 103(a) as being unpatentable over Himmelsbach (5736559, PTO-1449) would be maintained for reasons of record. The rejection would be applicable to new claims 19, 20.

Applicant argues that most of Himmelsbach's 300 example compounds are drawn to biphenyl containing a piperidinyl substituted with an aminocarbonyl or aminocarbonylalkyl, therefore Himmelsbach does not render the instant obvious. Applicant maintains that similar to the *In re Baird* situation, there is no suggestion within the disclosure of Himmelsbach to select the specific substituents which would result in the instant piperidinyl compound.

On the contrary, Himmelsbach discloses a broad genus of compounds and describes a large number of diverse example compounds covering different aspects of the genus. Each example would represent a preferred genus. Unlike the *In re Baird* situation, where the closest prior art compound of Knapp (column 4, lines 51-64; column 5, lines 36-39) and the example compound of Baird (Fig. 1) has several structural differences that one of ordinary skill in the art has to modify Knapp's compound via multiple changes to arrive at Baird's compound,

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Himmelsbach's Example 1 (6) on column 34 is within the most particularly preferred genus (column 5), and it differs from the instant in only one aspect, i.e. it has a methyl instead of the instant ethyl, propyl or benzyl on the amido nitrogen as R¹ and R². The instant compound is a homolog of Himmelsbach's example compound. To one of ordinary skill in the art, the homologs are expected to have similar activities. The prior art compound suggests the instant.

Furthermore, Himmelsbach, specifically teaches that methyl, ethyl, propyl, isopropyl and benzyl are optional choices within a small genus of compounds (column 2, line 33; lines 50-53). One of ordinary skill in the art would be motivated to replace Himmelsbach's methyl with the homologous ethyl, isopropyl or propyl, or the alternative benzyl to arrive at the instant invention with the reasonable expectation of obtaining an additional compound useful for inhibiting platelet aggregation since Himmelsbach had clearly taught that any species within the disclosed genus would be effective as anti-aggregation agent.

Applicant maintains that since Himmelsbach does not claim the 1-biphenyl-carbonyl, 4-aminocarbonyl- or 4-aminocarbonyl-substituted piperidinyl, it is not obvious to modify these compounds to arrive at the instant.

However, many reasons may account for these compounds not found in the claims. The absence of these compounds in the claims in this particular patent does not negate the positive teaching that they are among the most particularly preferred genus.

5. The rejection for Claims 1-3, 10, 12-15 under 35 U.S.C. 103(a) as being unpatentable over Sugimoto (4895841) would be maintained for reasons of record. The rejection is applicable to new claims 19, 20.

Applicant contends that only four of the 249 exemplified compounds of Sugimoto are drawn to a piperidinyl substituted with an aminocarbonylalkyl, and only one compound (Example 237 in column 107-108) contains two rings as in the instant. Therefore Sugimoto does not render the instant obvious. Applicant maintains that similar to the *In re Baird* situation, there is no suggestion within the disclosure of Sugimoto to select the specific substituents which would result in the instant piperidinyl compound.

On the contrary, Sugimoto discloses a broad genus of compounds and describes a large number of diverse example compounds covering different aspects of the genus. Each example

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therefore represents a preferred embodiment. Unlike the *In re Baird* situation, where the closest prior art compound of Knapp (column 4, lines 51-64; column 5, lines 36-39) and the example compound of Baird (Fig. 1) has several structural differences that one of ordinary skill in the art has to modify Knapp's compound via multiple changes to arrive at Baird's compound, Sugimoto's Example 49 on column 55-56 is within the preferred genus and it differs from the instant in only one aspect, i.e. Sugimoto's example compound 49 does not have phenylmethoxy on the phenyl as in the instant. However, Sugimoto teaches that the presence or absence of substituents on the phenyl is an optional choice (column 8, line 39 to column 9, line 1), an example of phenylmethoxy-substituted phenyl is shown on columns 107-108, Example 237. In view of Sugimoto's teaching, one of ordinary skill in the art would be motivated to replace Sugimoto's unsubstituted phenyl with the alternative, exemplified phenylmethoxy-phenyl to arrive at the instant invention with the reasonable expectation of obtaining an additional compound useful for inhibiting acetylcholinesterase and thereby useful for treating CNS disorder such as dementia.

Claim Rejections - 35 USC § 112(1)

6. The rejection for Claims 1-4, 10, 12-18 under 35 U.S.C. 112, first paragraph would be maintained for reasons of record, because the specification is only enabling for using the compounds of claims 5, 7-9 for treating emesis, pain depression or anxiety. The rejection is applicable to new claims 19, 20.

Applicant maintains that the examiner has not provided evidence that would cause the skilled artisan to doubt Applicant's teachings of utility. One of ordinary skill in the art would be able to use the compounds for the stated utility without undue experimentation.

Applicant has submitted data showing that the inventive compounds have NK-1 and NK-2 receptor binding activity. A Declaration under 37 C.F.R. Rule 1.132 would follow. However, these binding studies fails to distinguish the agonists from the antagonists. Furthermore, the nexus between the inhibition of the binding to the NK-1 or NK2 receptors and the treatment of the generic classes of diseases as recited in the instant claims (such as nervous system disorder, eating disorders, cerebrovascular diseases, neurodegenerative disorders, Alzheimer's disease etc,

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etc. which embraces conflicting diseases or conditions of diverse origins and causes), has not been established (Gao, Current Medicinal Chemistry, 1999, 6, 375-388). At present, there is no umbrella drug known to treat all the spectrum of diseases as cited in the instant.

The instant claims encompass compounds of vastly diverse structures, some quite removed from the examples. Because of the high degree of unpredictability in the art, one of ordinary skill in the art would have no basis to extrapolate the results to compounds structurally dissimilar to the examples, and expect that the variety of these structurally diverse compounds embraced by the claims would share the same biological activities. While some experimentation is permitted and every claimed embodiment need not be shown to possess the asserted activity, there should be a showing commensurate in scope with the claims. As stated in *In re Cavallito* 127, USPQ 202, “where the applicant seeks to obtain a monopoly in exchange for his disclosure of a group of compounds, there should be a disclosure which gives reasonable assurance that all, or substantially all of them are useful....an applicant is not entitled to a claim for a large group of compounds merely on the basis of a showing that a selected few are useful and a general suggestion of a similar utility in the others”. Furthermore, in the instant art, where there is a high degree of unpredictability exists, the required disclosure will be greater than for the disclosure of an invention involving a predictable factor such as a mechanical or electrical element. In *re Vaeck*, 20 USPQ 2d 1438.

In conclusion, in view of the state of the art, the high degree of unpredictability of the art, the limited working examples, the scope of the claims does not commensurate with that of the objective enablement. Insufficient teaching and guidance have not been provided in the specification to enable one of ordinary skill in the art to use the invention as claimed without undue experimentation

Allowable Subject Matter

7. Claims 5, 7-9 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims for reasons set forth in the previous office action.

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8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 571-272-0686. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alan Rotman can be reached on 571-272-0693. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Evelyn Huang

Primary Examiner

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